



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 01-1720)

RECEIVED
PATENT
JUN 18 2002
TECH CENTER 1600/2900
P#4

In re Application of:)
Asp, et al.)
Serial No.: 09/993,211) Examiner: TBA
Filed: November 16, 2001) Art Unit: 1614
For: Method for the Treatment of)
Cardiotoxicity Induced by Antitumor)
Compounds)

TRANSMITTAL LETTER

Asst. Commissioner for Patents
Washington, D.C. 20231

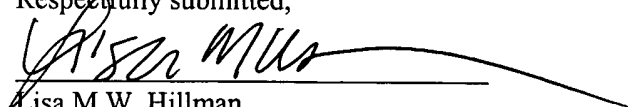
Dear Sir:

In regard to the above identified application,

1. We are transmitting herewith the attached:
 - a) Supplemental Information Disclosure Statement;
 - b) PTO Form 1449 and 30 cited references;
 - c) Return postcard
2. With respect to fees:
 - a) It is believed no fee is due at this time.
 - b) Please charge any underpayment or credit any overpayment our Deposit Account, No. 13-2490.
3. GENERAL AUTHORIZATION: Please charge any additional fees or credit overpayment to Deposit Account No. 13-2490. A duplicate copy of this sheet is enclosed.
4. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Asst. Commissioner for Patents, Washington, D.C. 20231 on June 5, 2002.

Date: June 5, 2002

Respectfully submitted,


Lisa M.W. Hillman

Registration No. 43,673



UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 01-1720)

PATENT

TECH CENTER 1600/2900

JUN 18 2002

RECEIVED

In the Application of:

Asp, et al.

Serial No.: **09/993,211**

Filed: **November 16, 2001**

For: **Method for the Treatment of
Cardiotoxicity Induced by Antitumor
Compounds**

Art Unit: 1614

Examiner: To be assigned

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Pursuant to the duty of disclosure provided by 35 C.F.R. § 1.56 and §§ 1.97-98, the applicants wish to make the following references of record in the above-identified application. Copies of the references are enclosed. Copies are also listed in the PTO-1449 form enclosed herewith. It is requested that the documents be given careful consideration and that they be cited of record in the prosecution history of the present application so that they will appear on the face of the patent issuing from the present application.

In the judgment of the undersigned, portions of the references may be material to the examination of the pending claims, however no such admission is intended. 37 C.F.R. 1.97 (h). The references have not been reviewed in sufficient detail to make any

other representation and, in particular, no representation is indented as to the relative importance of any portion of the references. This Statement is not a representation that the cited references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. sections 102 or 103.

CITED REFERENCES

Other Documents

- 1) Hasinoff, et al., "*Chemical, Biological and Clinical Aspects of Dexrazoxane and Other Bisdioxopiperazines*", *Current Medicinal Chemistry*, 5, p. 1-28, 1998
- 2) Lopez, et al., "*Randomized Prospective Clinical Trial of High-Dose Epirubicin and Dexrazoxane in Patients with Advanced Breast Cancer and Soft Tissue Sarcomas*", *J. Clin. Oncol.* Vol. 16, No. 1, pp. 86-92, 1998
- 3) Vici, et al., "*Dexrazoxane cardioprotection in advanced breast cancer patients undergoing high-dose epirubicin treatment*", *Clin. Ter.*, 149, pp. 15-20, 1998
- 4) Imondi, "*Preclinical Models of Cardiac Protection and Testing for Effects of Dexrazoxane on Doxorubicin Antitumor Effects*", *Semin. Oncol.* Vol. 25, No. 4, Suppl. 10, pp. 22-30, 1998
- 5) Lopez, et al., "*European Trials with Dexrazoxane in Amelioration of Doxorubicin and Epirubicin-Induced Cardiotoxicity*", *Semin. Oncol.* Vol. 25, No. 4, Suppl. 10, pp. 55-60, 1998
- 6) Hochster, "*Clinical Pharmacology of Dexrazoxane*", *Semin. Oncol.*, Vol. 25, No. 4, Suppl. 10, pp. 37-42, 1998
- 7) Von Hoff, "*Phase I Trials of Dexrazoxane and Other Potential Applications for the Agent*", *Semin. Oncol.*, Vol. 25, No. 4, Suppl. 10, pp. 31-36, 1998
- 8) Hellmann, "*Overview and Historical Development of Dexrazoxane*", *Semin. Oncol.*, Vol. 25, No. 4, Suppl. 10, pp. 48-54, 1998
- 9) Wexler, "*Ameliorating Anthracycline Cardiotoxicity in Children with Cancer: Clinical Trials with Dexrazoxane*", *Semin. Oncol.*, Vol. 25, No. 4, Suppl. 10, pp. 86-92, 1998
- 10) Synold, et al., "*Antineoplastic Activity of Continuous Exposure to Dexrazoxane: Potential New Role as a Novel Topoisomerase II Inhibitor*", *Semin. Oncol.*, Vol.

25, No. 4, Suppl. 10, pp. 93-99, 1998

- 11) Wiseman, et al., *"Dexrazoxane: A Review of its Use as a Cardioprotective Agent in Patients Receiving Anthracycline-Based Chemotherapy"*, *Drugs*, 56 (3): pp. 385-403, 1998
- 12) Della Torre, et al., *"Protection against doxorubicin-induced cardiotoxicity in weanling rats by dexrazoxane"*, *Cancer Chemother Pharmacol*, 43, pp. 151-156, 1999
- 13) O'Donnell, et al., *"A Phase I Trial of the VEGF Inhibitor SU5416, Incorporating Dynamic Contrast MRI Assessment of Vascular Permeability"*, *685, *Proceedings of ASCO, Clinical Pharmacology*, Volume 19, p. 177a, 2000
- 14) Baselga, et al., *"Continuous Administration of ZD1839 (Iressa), a Novel Oral Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor (EGFR-TKI), in Patients with Five Selected Tumor Types: Evidence of Activity and Good Tolerability"*, *686, *Proceedings of ASCO, Clinical Pharmacology*, Volume 19, p. 177a, 2000
- 15) Stewart, et al., *"Population Pharmacokinetics of Topotecan in Children and Adolescents"*, *687, *Proceedings of ASCO, Clinical Pharmacology*, Volume 19, p. 177a, 2000
- 16) Lewis, et al., *"A Phase-I Study of the Novel Topoisomerase-I Inhibitor J-107088 Administered on a Multiple-Dose Schedule"*, *688, *Proceedings of ASCO, Clinical Pharmacology*, Volume 19, p. 177a, 2000
- 17) Garrison, et al., *"A Phase I and Pharmacokinetic Study of the Camptothecin (CPT) Analog DX-89511 (Exetecan Mesylate): Escalating Infusion Duration and Dose"*, *765, *Proceedings of ASCO, Clinical Pharmacology*, Volume 19, p. 197a, 2000
- 18) Houghton, et al., *"Anticancer Activity of the Novel DB-67 Silatecan, a Highly Lipophilic Liposomal Camptothecin Agent Displaying Improved Intrinsic Human Blood and Plasma Stability and Potent Topoisomerase I Activity"*, *766, *Proceedings of ASCO, Clinical Pharmacology*, Volume 19, p. 197a, 2000
- 19) Peck, *Phase I Trial of J-107088, a Novel Topoisomerase I Inhibitor, Administered Once Every 21 Days*, *767, *Proceedings of ASCO, Clinical Pharmacology*, Volume 19, p. 197a, 2000
- 20) Bos, et al., *"Phase I Study of NX 211 (Liposomal Lurtotecan) Administered as a Single Dose Every 3 Weeks"*, *768, *Proceedings of ASCO, Clinical Pharmacology*, Volume 19, p. 197a, 2000

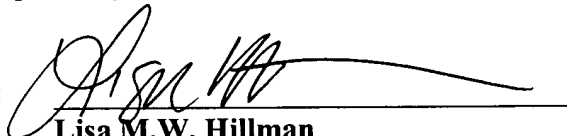
- 21) Swain, et al., "*Cardioprotection with Dexrazoxane for Doxorubicin-Containing Therapy in Advanced Breast Cancer*", *Journal of Clinical Oncology*, Vol. 15, No. 4, pp. 1318-1332, 1997
- 22) Gianni, "*Tolerability in patients receiving trastuzumab with or without chemotherapy*", *Annals of Oncology*, 12 (Suppl. 1): S63-S68, 2001
- 23) Imondi, et al., "*Dose-response relationship of dexrazoxane for prevention of doxorubicin-induced cardiotoxicity in mice, rats, and dogs*", *Cancer Research*, Abstract, 56 (18):4200, 1996
- 24) Baldwin, et al., "*Dose-Independent Pharmacokinetics of the Cardioprotective Agent Dexrazoxane in Dogs*", *Biopharmaceutics & Drug Disposition*, Article Abstract, Vol. 17, Issue 6, pp. 541-550, 1996
- 25) Malisza, et al., "*Inhibition of Anthracycline Semiquinone Formation by ICRF-187 (Dexrazoxane) in cells*", *Free Radical Biology & Medicine*, Vol. 20, No. 7, pp. 905-914, 1996
- 26) Bates, et al., "*A Pharmacoeconomic Evaluation of the Use of Dexrazoxane in Preventing Anthracycline-Induced Cardiotoxicity in Patients with Stage IIB or IV Metastatic Breast Cancer*", *Clinical Therapeutics*, Vol. 19, No. 1, pp. 167-184 1997
- 27) Woodlock, et al., "*Coincident Acute Myelogenous Leukemia and Ischemic Heart Disease: Use of the Cardioprotectant Dexrazoxne During Induction Chemotherapy*", *American Journal of Hematology*, 59, pp. 246-248 1998
- 28) Sawyer, et al., "*Daunorubicin-Induced Apoptosis in Rat Cardiac Myocytes is Inhibited by Dexrazoxane*", *Original Contributions*, pp.257-265, © American Heart Association, Inc. 1999
- 29) Ohkubo, et al., "*Synthesis and Biological Activities of NB-506 Analogues Modified at the Glucose Group*", *Bioorganic & Medicinal Chemistry Letters*, Vol. 10, pp. 419-422, 2000

- 30) Long, et al., *"Non-camptothecin topoisomerase I active compounds as potential anticancer agents"*, *Expert Opinion on Therapeutic Patents*, 10(5), pp. 635-666, 2000

Respectfully submitted,

Date: June 5, 2002

by:

A handwritten signature in dark ink, appearing to read 'Lisa M.W. Hillman', written over a horizontal line.

Lisa M.W. Hillman

Reg. No. 43,673

8	Hellmann, "Overview and Historical Development of Dexrazoxane", <i>Semin. Oncol.</i> , Vol. 25, No. 4, Suppl. 10, pp. 48-54, 1998
9	Wexler, "Ameliorating Anthracycline Cardiotoxicity in Children with Cancer: Clinical Trials with Dexrazoxane", <i>Semin. Oncol.</i> , Vol. 25, No. 4, Suppl. 10, pp. 86-92, 1998
10	Synold, et al., "Antineoplastic Activity of Continuous Exposure to Dexrazoxane: Potential New Role as a Novel Topoisomerase II Inhibitor", <i>Semin. Oncol.</i> , Vol. 25, No. 4, Suppl. 10, pp. 93-99, 1998
11	Wiseman, et al., "Dexrazoxane: A Review of its Use as a Cardioprotective Agent in Patients Receiving Anthracycline-Based Chemotherapy", <i>Drugs</i> , 56 (3): pp. 385-403, 1998
12	Della Torre, et al., "Protection against doxorubicin-induced cardiotoxicity in weanling rats by dexrazoxane", <i>Cancer Chemother Pharmacol</i> , 43, pp. 151-156, 1999
13	O'Donnell, et al., "A Phase I Trial of the VEGF Inhibitor SU5416, Incorporating Dynamic Contrast MRI Assessment of Vascular Permeability", *685, <i>Proceedings of ASCO, Clinical Pharmacology</i> , Volume 19, p. 177a, 2000
14	Baselga, et al., "Continuous Administration of ZD1839 (Iressa), a Novel Oral Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor (EGFR-TKI), in Patients with Five Selected Tumor Types: Evidence of Activity and Good Tolerability", *686, <i>Proceedings of ASCO, Clinical Pharmacology</i> , Volume 19, p. 177a, 2000
15	Stewart, et al., "Population Pharmacokinetics of Topotecan in Children and Adolescents", *687, <i>Proceedings of ASCO, Clinical Pharmacology</i> , Volume 19, p. 177a, 2000
16	Lewis, et al., "A Phase-I Study of the Novel Topoisomerase-I Inhibitor J-107088 Administered on a Multiple-Dose Schedule", *688, <i>Proceedings of ASCO, Clinical Pharmacology</i> , Volume 19, p. 177a, 2000
17	Garrison, et al., "A Phase I and Pharmacokinetic Study of the Camptothecin (CPT) Analog DX-89511 (Exetecan Mesylate): Escalating Infusion Duration and Dose", *765, <i>Proceedings of ASCO, Clinical Pharmacology</i> , Volume 19, p. 197a, 2000
18	Houghton, et al., "Anticancer Activity of the Novel DB-67 Silatecan, a Highly Lipophilic Liposomal Camptothecin Agent Displaying Improved Intrinsic Human Blood and Plasma Stability and Potent Topoisomerase I Activity", *766, <i>Proceedings of ASCO, Clinical Pharmacology</i> , Volume 19, p. 197a, 2000
19	Peck, Phase I Trial of J-107088, a Novel Topoisomerase I Inhibitor, Administered Once Every 21 Days", *767, <i>Proceedings of ASCO, Clinical Pharmacology</i> , Volume 19, p. 197a, 2000
20	Bos, et al., "Phase I Study of NX 211 (Liposomal Lurtotecan) Administered as a Single Dose Every 3 Weeks", *768, <i>Proceedings of ASCO, Clinical Pharmacology</i> , Volume 19, p. 197a, 2000
21	Swain, et al., "Cardioprotection with Dexrazoxane for Doxorubicin-Containing Therapy in Advanced Breast Cancer", <i>Journal of Clinical Oncology</i> , Vol. 15, No. 4, pp. 1318-1332, 1997
22	Gianni, "Tolerability in patients receiving trastuzumab with or without chemotherapy", <i>Annals of Oncology</i> , 12 (Suppl. 1): S63-S68, 2001
23	Imondi, et al., "Dose-response relationship of dexrazoxane for prevention of doxorubicin-induced cardiotoxicity in mice, rats, and dogs", <i>Cancer Research</i> , Abstract, 56 (18):4200, 1996
24	Baldwin, et al., "Dose-Independent Pharmacokinetics of the Cardioprotective Agent Dexrazoxane in Dogs", <i>Biopharmaceutics & Drug Disposition</i> , Article Abstract, Vol. 17, Issue 6, pp. 541-550, 1996
25	Maliszka, et al., "Inhibition of Anthracycline Semiquinone Formation by ICRF-187 (Dexrazoxane) in cells", <i>Free Radical Biology & Medicine</i> , Vol. 20, No. 7, pp. 905-914, 1996
26	Bates, et al., "A Pharmacoeconomic Evaluation of the Use of Dexrazoxane in Preventing Anthracycline-Induced Cardiotoxicity in Patients with Stage IIB or IV Metastatic Breast Cancer", <i>Clinical Therapeutics</i> , Vol. 19, No. 1, pp. 167-184 1997
27	Woodlock, et al., "Coincident Acute Myelogenous Leukemia and Ischemic Heart Disease: Use of the Cardioprotectant Dexrazoxane During Induction Chemotherapy", <i>American Journal of Hematology</i> , 59, pp. 246-248 1998
28	Sawyer, et al., "Daunorubicin-Induced Apoptosis in Rat Cardiac Myocytes is Inhibited by Dexrazoxane", <i>Original Contributions</i> , pp.257-265, © American Heart Association, Inc. 1999
29	Ohkubo, et al., "Synthesis and Biological Activities of NB-506 Analogues Modified at the Glucose Group", <i>Bioorganic & Medicinal Chemistry Letters</i> , Vol. 10, pp. 419-422, 2000
30	Long, et al., "Non-camptothecin topoisomerase I active compounds as potential anticancer agents", <i>Expert Opinion on Therapeutic Patents</i> , 10(5), pp. 635-666, 2000

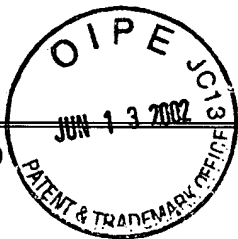
EXAMINER

DATE CONSIDERED

RECEIVED

JUN 18 2002

TECH CENTER 1600/2900

FORM PTO-1449
(R v. 2-32)U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket N .

01-1720

S rial No.

09/993,211

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT
(Use several sheets if necessary)

Applicant:

Asp, et al.

Filing Date:

November 16, 2001

Group:

1614

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

	Document Number	Date	Country	Class	Subclass	Translation	
						Yes	No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).

1	Hasinoff, et al., "Chemical, Biological and Clinical Aspects of Dexrazoxane and Other Bisdioxopiperazines", <i>Current Medicinal Chemistry</i> , 5, p. 1-28, 1998
2	Lopez, et al., "Randomized Prospective Clinical Trial of High-Dose Epirubicin and Dexrazoxane in Patients with Advanced Breast Cancer and Soft Tissue Sarcomas", <i>J. Clin. Oncol.</i> Vol. 16, No. 1, pp. 86-92, 1998
3	Vici, et al., "Dexrazoxane cardioprotection in advanced breast cancer patients undergoing high-dose epirubicin treatment", <i>Clin. Ter.</i> , 149, pp. 15-20, 1998
4	Imondi, "Preclinical Models of Cardiac Protection and Testing for Effects of Dexrazoxane on Doxorubicin Antitumor Effects", <i>Semin. Oncol.</i> Vol. 25, No. 4, Suppl. 10, pp. 22-30, 1998
5	Lopez, et al., "European Trials with Dexrazoxane in Amelioration of Doxorubicin and Epirubicin-Induced Cardiotoxicity", <i>Semin. Oncol.</i> Vol. 25, No. 4, Suppl. 10, pp. 55-60, 1998
6	Hochster, "Clinical Pharmacology of Dexrazoxane", <i>Semin. Oncol.</i> , Vol. 25, No. 4, Suppl. 10, pp. 37-42, 1998
7	Von Hoff, "Phase I Trials of Dexrazoxane and Other Potential Applications for the Agent", <i>Semin. Oncol.</i> , Vol. 25, No. 4, Suppl. 10, pp. 31-36, 1998

RECEIVED
JUN 18 2002
TECH CENTER 1600/2900

--	--

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

RECEIVED
JUN 18 2002
TECH CENTER 1600/2900

THIS PAGE BLANK (USPTO)